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Hybrid coronary revascularization versus conventional coronary artery bypass grafting

Systematic review and meta-analysis

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Abstract

Background: Hybrid coronary revascularization (HCR) combining minimally invasive grafting of the left internal mammary artery to the left anterior descending artery with percutaneous coronary intervention has become a viable option for treating coronary artery disease. The aim of this meta-analysis was to compare HCR with conventional coronary artery bypass grafting (CABG) in a range of clinical outcomes and hospital costs.

Methods: To identify potential studies, systematic searches were carried out in various databases. The key search terms included “hybrid revascularization” AND “coronary artery bypass grafting” OR “HCR” OR “CABG.” This was followed by a meta-analysis investigating the need for blood transfusion, hospital costs, ventilation time, hospital stay, cerebrovascular accident, myocardial infarction, mortality, postoperative atrial fibrillation, renal failure, operation duration, and ICU stay.

Results: The requirement for blood transfusion was significantly lower for HCR: odds ratio 0.38 (95% confidence intervals [CIs] 0.31–0.46, $P<.00001$) as was the hospital stay: mean difference (MD) −1.48 days (95% CI, −2.61 to −0.36, $P=0.01$) and the ventilation time: MD −8.99 hours (95% CI, −15.85 to −2.13, $P=.01$). On the contrary, hospital costs were more expensive for HCR: MD $3970 (95% CI, 2570–5370, $P<.00001$). All other comparisons were insignificant.

Conclusions: In the short-term, HCR is as safe as conventional CABG and may offer certain benefits such as a lower requirement for blood transfusion and shorter hospital stays. However, HCR is more expensive than conventional CABG.

Abbreviations: CABG = coronary artery bypass grafting, CI = confidence interval, CVA = cerebrovascular accident, DES = drug eluting stent, HCR = hybrid coronary revascularization, ICU = intensive care unit, LAD = left anterior descending artery, LIMA = left internal mammary artery, LITA = left internal thoracic artery, MACE/MACCE = major adverse cardiac events/major adverse cardiac and cerebrovascular events, MD = mean difference, MI = myocardial infarction, OR = odds ratio, PCI = percutaneous coronary intervention, POAF = postoperative atrial fibrillation, SVG = saphenous vein graft.

Keywords: blood transfusion, cardiac surgery, coronary artery disease, hospital costs, percutaneous coronary intervention

1. Introduction

When comparing coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI) for the treatment of triple vessel or left main stem disease, the long-term results of various randomized controlled trials support the use of CABG (e.g., SYNTAX;[1] BARI;[2] FREEDOM).[3] One of the reasons for CABG’s superiority is the gold standard approach of bypassing the left anterior descending artery (LAD) using the left internal mammary artery (LIMA, also known as the left internal thoracic artery [LITA]). Indeed, studies have reported 10-year patency rates from 95% to 98%.[4] An increasingly attractive proposition is to operate using minimally invasive techniques with a likely reduction in wound infection[5] and shorter ICU stays.[6]

For lesions affecting non-LAD arteries, the saphenous vein (SVG) can be the preferred conduit for CABG. However, SVGs are not as robust as arterial conduits and an average failure rate of 20% at 1 year and 40% to 50% at 10 to 15 years has been reported.[4] In contrast in recent clinical trials the newer drug eluting stents (DES) have been associated with a 3.9% restenosis rate at 2 years and 5.9% target lesion revascularization rate at 4 years.[7] This favorable comparison combined with reduced invasiveness supports the use of percutaneous coronary intervention (PCI) in non LAD lesions.

The aim of hybrid coronary revascularization (HCR) is to combine minimally invasive LITA to LAD CABG with PCI for the other lesion(s). The first HCR was performed by Angelini et al in 1996.[8] The technique consisted of the combination of percutaneous transluminal coronary angioplasty with anastomoses of LITA to LAD via a small left anterior thoracotomy. Six patients underwent the procedure: 4 in a 2-stage process and 2 in a simultaneous process. Afterward, all patients were reported to be free from symptoms.[8] Increased interest in the approach occurred with the advent of DES in the 2000s and between 2001

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and 2016 twelve studies comparing HCR vesus conventional CABG were carried out. Possible benefits of HCR compared with CABG included a lower requirement for blood transfusion[9–10] and a shorter hospital stay.[11–12]

There have been 3 previous meta-analyses[13–15] comparing CABG versus HCR; however, none of them include as many studies as this one and none of them investigated the important outcome, hospital cost. Therefore, the aim of this meta-analysis was to provide a more comprehensive representation of all available studies (14 included) and all available outcomes (11 included) to reach a conclusion about whether either approach is clinically superior. The objective was to investigate whether there was any superiority to treating adult patients with coronary artery disease with HCR compared with conventional CABG. The outcomes investigated were blood transfusion (number of participants requiring); hospital cost; ventilation time; hospital stay; cerebrovascular accident; myocardial infarction (MI); mortality; postoperative atrial fibrillation (POAF); renal failure; operation duration; and ICU stay.

2. Methods

2.1. Ethical approval

This study involves pooling and synthesis of data from published research. As such no humans or animals were utilized and therefore no ethical approval was required.

2.2. Search strategy

To identify potential studies, systematic searches were carried out using the following databases: EMBASE, PubMed, Web of Science, and the Cochrane Central Registry of Controlled Trials (CENTRAL). The search was supplemented by scanning the reference lists of eligible studies. The search strategy included the key concepts of "hybrid coronary revascularization" AND "coronary artery bypass grafting" OR "HCR" OR "CABG." The details of the PubMed search are presented in the supplementary files, http://links.lww.com/MD/C414. All identified papers were assessed independently by 2 reviewers. Searches of published papers were conducted up until September 25, 2017.

2.3. Types of studies to be included and excluded

All trials of patients undergoing HCR versus CABG were included. There were no language restrictions. Animal studies were excluded. Studies that did not have any of the desired outcome measures were excluded. Incomplete data, or data from an already included study, were excluded. Other treatment modalities and interventions for coronary artery disease such as percutaneous coronary intervention were only present in one of the included studies, where HCR, CABG, and PCI were compared with one another; in this case, the data for CABG and HCR were extracted and the PCI sample excluded.[16] Data extraction was performed by AR with double checking by NK.

2.4. Participants/population

This meta-analysis analyzed all trials of both male and female adult (≥18 years) patients with coronary artery disease who were undergoing myocardial reperfusion using either HCR or conventional CABG (treating multiple sites of atherosclerosis with individual grafts).

2.5. Intervention(s), exposure(s)

This meta-analysis considered all trials where patients with stable angina or acute coronary syndrome were exposed to either HCR or conventional CABG. More specifically, all trials, where the intervention of combining PCI with CABG for the treatment of myocardial ischemia, were used.

2.6. Search results

Our initial search found 348 articles. Of these 323 studies were excluded on the basis of title and abstract. This left 25 studies. Of these studies we excluded 8 studies because they had no comparator group; 1 study because it was a single case study; 1 study because it only reported long-term outcomes; and 1 study because it reported HCR versus percutaneous coronary intervention (Supplementary Figure S1, http://links.lww.com/MD/C414). Fourteen studies were included in our analysis.[9–13,16,17–25]

2.7. Outcome(s)

The primary outcomes analyzed were blood transfusion (number of participants requiring); hospital cost; ventilation time; hospital stay; cerebrovascular accident; MI; mortality; postoperative atrial fibrillation (POAF); renal failure; operation duration; and ICU stay.

2.8. Risk of publication bias

Risk of publication bias was assessed using funnel plots.[26]

2.9. Quality of included studies

The Newcastle Ottawa Scale was used to assess study quality (http://www.ohri.ca/programs/clinical_epidemiology/nosgen.doc). The results are displayed in Supplementary Table S2, http://links.lww.com/MD/C414.

2.10. Strategy for data synthesis

Odds ratios were calculated for dichotomous data using the Mantel–Haenszel method. An odds ratio (OR) is a measure of association between an exposure and an outcome. The OR represents the odds that an outcome will occur given a particular exposure, compared with the odds of the outcome occurring in the absence of that exposure. Mean differences were calculated for continuous data. Meta-analyses were completed for continuous data by calculating the mean difference between intervention and control groups from postintervention data only. It is an accepted practice to only use postintervention data for meta-analysis, but this method assumes that random allocation of participants always creates intervention groups matched at baseline for age, disease severity, where necessary median and ranges were converted to mean and standard deviation.[27] All analyses were conducted using Revman 5.3 (Nordic Cochrane Centre, Denmark). Heterogeneity was quantified using the I^2 test,[28] where a high percentage suggests significant heterogeneity and 0% no heterogeneity. In the presence of high heterogeneity, we used a random-effects model, otherwise a fixed-effects model was used. We used a 5% level of significance and 95% confidence intervals (CIs); figures were produced using Revman 5.3.

3. Results

The 14 studies (15 intervention groups) included in the analyses had an aggregate of 4260 participants, 1350 of which had HCR and 2910 had conventional CABG. Table 1 summarizes the

Table 1

Characteristics of included studies.

Study	HCR approach	CABG approach	n HCR (CABG)	Age HCR (CABG)	% Male HCR (CABG)	<30 d Outcome measures
Bachinsky et al (2012) USA	Robotic-assisted LIMA and/ or RIMA takedown. Anterior chest wall incision Either BMS or DES	Off pump	25 (27)	63.2 ± 10.5 (66.78 ± 10.7)	80 (59)	Blood transfusion Hospital costs Hospital stay ICU stay MI Mortality Operation time Pain Patient satisfaction POAF Stroke Time to return to work\normal Troponin
De Canniere et al (2001) Belgium	Minimally invasive LIMA to LAD Either BMS or DES	On-pump	20 (20)	62 ± 9 (63 ± 13)	80 (75)	Atrial fibrillation Blood transfusion Leg wound dehiscence Mobility \ independence Myocardial damage or infarction Pericardial effusion Pleural effusion Stroke
Delhaye et al (2010) France	LIMA to LAD, RIMA to non-LAD DES	Left to surgeon's preference	18 (18)	62 (60)	77.8 (77.8)	Blood transfusion Hospital Stay MI Mortality
Gasior et al (2014) France	LIMA to LAD MIDCAB/ EACAB DES	Left to surgeon's preference	98 (102)	63.1 ± (63.9 ± 8.4)	79.6 (71.6)	Blood transfusion MI Mortality
Halkos et al (2011) USA	LIMA to LAD EACAB DES	Off pump	147 (588)	64.3 ± 12.8 (64.3 ± 12.5)	61.9 (71.4)	Blood transfusion Hospital stay ICU stay MI Mortality POAF Renal failure Stroke Ventilation Time
Harskamp et al (2015) USA	LIMA to LAD EACAB DES	Left to surgeon's preference	306 (918)	64.6 ± 11.6 (64.8 ± 10.4)	70.3 (67.4)	Access site Blood transfusion Chest tube drainage Infection MI Mortality Operation time Renal failure Stroke
Hu et al (2011) China	LITA to LAD MIDCAB Not reported	Off pump	104 (104)	61.8 ± 10.2 (62.4 ± 8.0)	99.3 (79.8)	Blood transfusion Hospital costs Hospital stay ICU stay Infection MI Mortality Operation time POAF
Kon et al (2008) USA	LITA to LAD anterior lateral minithoracotomy DES	Off pump	15 (30)	61 ± 10 (65 ± 10)	73 (63)	Blood transfusion Hospital stay ICU stay Intraoperative cost MI Mortality Pain Renal insufficiency Stroke Ventilation time
Leacche et al (2013) USA	LIMA to LAD assumed DES assumed	On-pump	SYNTAX score <3267 (226) SYNTAX score >3213 (75)	62 (63) 74 (62)	79 (75) 62 (83)	Blood transfusion Hospital stay Mortality Operation time PLCOS POAF Renal failure Stroke
Reicher et al (2008) USA	LIMA to LAD anterior lateral small thoracotomy DES	Off pump	13 (26)	62 ± 10 (64 ± 10)	80 (83)	Blood loss Blood transfusion Hospital stay ICU stay Mortality Ventilation Time

(*continued*)

Table 1
(continued).

Study	HCR approach	CABG approach	n HCR (CABG)	Age HCR (CABG)	% Male HCR (CABG)	<30 d Outcome measures
Shen et al (2013) China	LIMA to LAD Ministernotomy	Surgeon's preference	141 (141)	62.0 ± 9.9 (62.4 ± 7.8)	88.7% (90.1%)	Death MI Neurologic event repeat revascularization "Any MACCE"
Song et al (2016) China	LIMA to LAD MIDCAB 99.5% DES	Off pump	120 (240)	62.3 ± 9.4 (62.8 ± 8.4)	80.8 (79.6)	Blood transfusion Hospital stay ICU stay Ventilation time
Zhao et al (2001) USA	LIMA to LAD DES	Both	122 (254)	(Median) 63 (63)		Blood transfusion Chest tube drainage CK:MB Creatine New renal failure POAF Revision for bleeding Stroke Deep sternal wound infection Hospital stay Intra-aortic balloon pump Intrastent thrombosis Mortality New low cardiac output syndrome
Zhou et al (2014) China	LIMA to LAD MIDCAB Not reported	Off pump	141 (141)	62 ± 10.1 (63.2 ± 8.5)	88.7 (89.4)	Atelectasis Blood transfusion Hospital stay ICU stay Intraaortic balloon pump Mortality Myocardial damage Operation time POAF Renal failure Stroke Ventilation time

BMS = bare metal stent, CABG = coronary artery bypass grafting, CK-MB = creatine kinase, muscle brain band, DES = drug eluting stent, EACAB-HCR = hybrid coronary revascularization, ICU = intensive care unit, LAD = left anterior descending artery, LIMA = left internal mammary artery, LITA = left internal thoracic artery, MACCE = major adverse cardiac or cerebrovascular events, MI = myocardial infarction, MIDCAB = minimally invasive coronary artery bypass surgery, PLCOS = postoperative low cardiac output syndrome, POAF = postoperative atrial fibrillation, RIMA = right internal mammary artery.

characteristics of the included studies. Supplementary Table S1, http://links.lww.com/MD/C414 lists the excluded trials and reasons for exclusion.

3.1. Blood transfusion

Ten studies reported the incidence of blood transfusion. Overall, 22.8% of HCR patients received a blood transfusion compared with 46.1% of the CABG group. The odds ratio (OR) for the pooled analysis was OR 0.38 (95% CI, 0.31–0.46, I^2 = 48%, P < .00001; Fig. 1). The odds of requiring a blood transfusion were significantly lower in the patients who underwent HCR compared with the odds of those who underwent CABG.

3.2. Hospital costs (thousands of US dollars)

Four studies examined the hospital costs of each procedure in US dollars, which was converted to thousands of US dollars, to allow

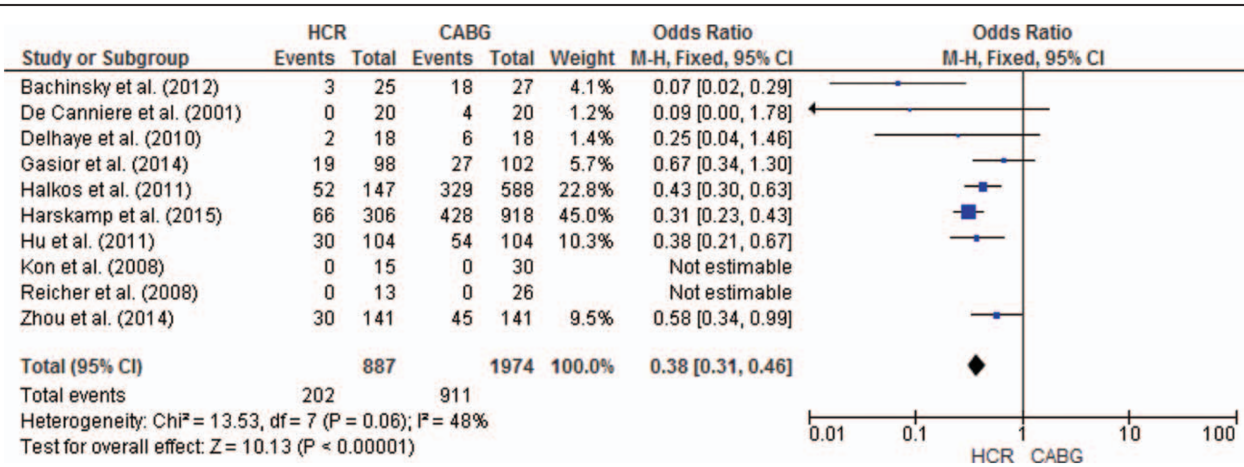

Figure 1. Requirement for blood transfusion.

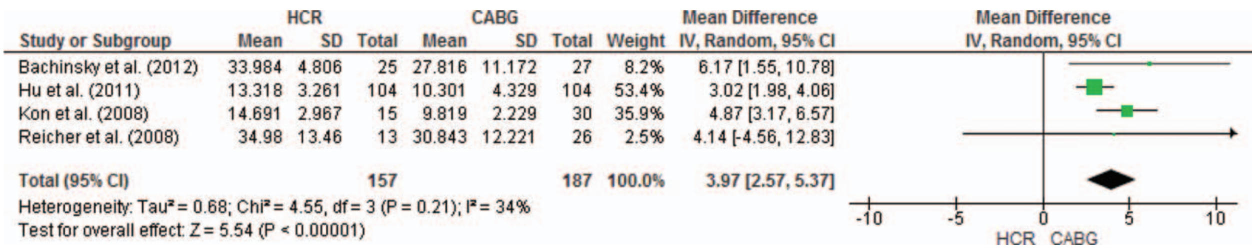

Figure 2. Hospital costs.

for a more comprehensive forest plot. The mean difference (MD) for the pooled analysis was 3.97 thousand US dollars (95% CI, 2.57–5.37, $I^2=34\%$, $P<.00001$; Fig. 2). The hospital cost for CABG was significantly lower than for HCR.

3.3. Ventilation time

Five studies reported intubation (mechanical ventilation) time in hours for both procedures. The MD for the pooled analysis was −8.99 hours (95% CI, −15.85 to −2.13, $I^2=96\%$, $P=.01$; Fig. 3). There was a longer duration of mechanical ventilation after CABG compared with HCR.

3.4. Hospital stay (days)

Six studies examined the postoperative length of stay of patients in days. The MD for the pooled analysis was −1.48 days (95% CI, −2.61 to −0.36, $I^2=84\%$, $P=.010$; Fig. 4). There was a significantly shorter length of postoperative stay in hospital after the HCR procedure than after CABG.

3.5. Cerebrovascular accident

Eight studies (9 intervention groups) examined the incidence of cerebrovascular accident (CVA). The incidence of CVA in the HCR group was 0.9% compared with 1.4% in the CABG group. The OR for the pooled analysis was 0.72 (95% CI, 0.31–1.69, $I^2=0\%$, $P=.45$; Figure S2, http://links.lww.com/MD/C414). There were equal odds for the incidence of CVA in both groups.

3.6. MI

Nine studies examined the incidence of both peri- and postoperative MI in the 2 procedures. 3.2% of patients treated with HCR suffered a MI compared with 2.6% of patients undergoing CABG. The OR for the pooled analysis was 0.54 (95% CI, 0.28–1.02, $I^2=4\%$, $P=.06$; Figure S3, http://links.lww.com/MD/C414). There was no significant difference in the odds of having an MI in the HCR or CABG groups.

3.7. Mortality

Twelve studies (13 intervention groups) investigated the incidence of mortality in both procedures. The incidence of mortality in the HCR group was 1.7% as opposed to the CABG where the incidence was 1.8%. The OR for the pooled analysis was 1.15 (95% CI, 0.69–1.92, $I^2=20\%$, $P=.59$; Figure S4, http://links.lww.com/MD/C414). There was no significant

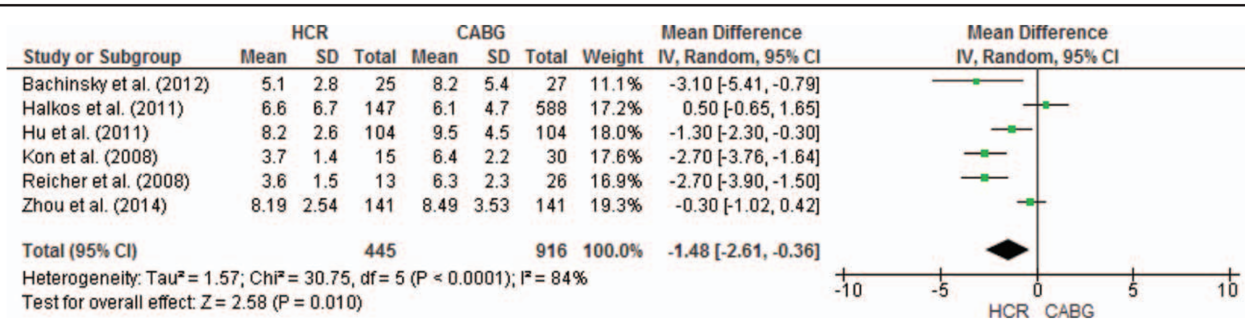

Figure 3. Ventilation time.

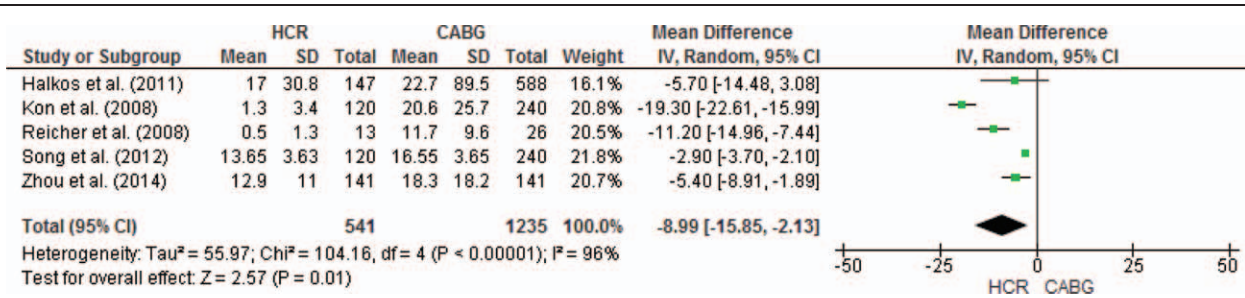

Figure 4. Hospital stay.

difference in the odds of mortality in the HCR group compared with the CABG group.

3.8. Postoperative atrial fibrillation

Seven studies (8 intervention groups) examined the incidence of postoperative Atrial Fibrillation (POAF). In the HCR group, the incidence of POAF was 17%, compared with 19.2% in the CABG group. The OR for the pooled analysis was 0.96 (95% CI, 0.74–1.24, $I^2=35\%$, $P=.74$; Figure S5, http://links.lww.com/MD/C414). There was no difference in the odds of POAF occurring in the HCR group compared with the CABG group.

3.9. Renal failure

Five studies (6 intervention groups) reported the incidence of renal failure. In the HCR group, there was a renal failure incidence of 1.7%, compared with 2.6% in the CABG group. The OR for the pooled analysis was 0.73 (95% CI, 0.39 to 1.36, $I^2=0\%$, $P=.32$; Figure S6, http://links.lww.com/MD/C414). There was no difference in the odds of renal failure happening in either the HCR or CABG group.

3.10. Operation time (minutes)

Four studies examined the operation times for both procedures. The MD for the pooled analysis was 46.17 minutes (95% CI, −13.88 to 106.22, $I^2=98\%$, $P=.13$; Figure S7, http://links.lww.com/MD/C414). There was no significant difference between the operation time for HCR versus that for CABG.

3.11. ICU stay (hours)

Seven studies examined the length of stay of patients in the intensive care unit (hours) after their procedure. The MD for the pooled analysis was −40.85 hours (95% CI, −85.63 to 3.94, $I^2=99\%$, $P=.07$; Figure S8, http://links.lww.com/MD/C414). There was no significant difference in the length of stay in ICU between the 2 groups.

3.12. Leave one out/sensitivity analysis

A sensitivity analysis was carried out on all the significant results. In the cases of requirement for blood transfusion, hospital costs and hospital stay leaving out any single study still left a significant result. When Reicher et al[12] were omitted from the ventilation time analysis, the P value became .05.

3.13. Publication bias

The funnel plots for requirement for blood transfusion, incidence of myocardial infarction and postoperative atrial fibrillation were symmetrical. All other funnel plots were nonsymmetric.

3.14. Study quality

According to the Newcastle Otawa Scale, most of the studies were of reasonable quality with scores ranging from 7* to 8* out of a maximum attainable score of 9*.

4. Discussion

A combination of the LIMA to LAD coronary artery bypass with percutaneous coronary intervention for other coronary lesions has become a viable option. The aim of this meta-analysis was to investigate how this hybrid approach compared with conventional CABG using a range of clinical outcomes and also investigating hospital cost. The results showed that the requirement for blood transfusion, hospital stay, and ventilation time significantly favored HCR, whereas conventional CABG was cheaper in terms of hospital costs and all other comparisons were insignificant. This suggests that HCR has some advantages compared with conventional CABG, but conventional CABG is the cheaper option.

Accompanying PCI with dual antiplatelet therapy is standard practice. Due to concerns about bleeding complications it can be preferred to perform the LIMA to LAD surgery first and then carry out PCI.[9] This indeed appeared to be the case as in almost all of the included studies CABG was carried out first[9–12,16–17,19–25] except when the non-LAD lesion was critical.[10] In the majority of the included studies, surgery and PCI were carried out on the same day.[9–12,16–17,21,23–25] In which case administration of clopidogrel occurred soon after surgery had taken place. Yet in spite of this, the requirement for blood transfusion was consistently lower in the HCR group. This is consistent with the findings of other meta-analyses.[13–15] The reason for this is thought to be the less invasive and traumatic nature of the minimally invasive techniques used for the LIMA to LAD surgery compared with a full sternotomy used in conventional CABG.[21]

The subject of hospital costs is controversial and involves trying to balance best patient outcomes with value for money. In all of the studies that investigated costs these were higher for HCR, although in Reicher et al[12] the difference was insignificant. The greater cost for HCR could mainly be due to the use of radiographic instruments and stent implantation.[21] It has been suggested that with increasing experience such costs may decrease, particularly when combined with the shorter hospital stay.[17] It should also be noted the time taken for the patient to return to work was significantly shorter after HCR compared with conventional CABG.[17]

The clinical outcomes: incidence of CVA, MI occurrence, mortality, incidence of POAF, and incidence of renal failure were all insignificant at <30 days. Not surprisingly, this correlated well with those authors who measured MACE/MACCE,[9,11–12,16–17,19–20,23] although Leacche et al[22] found that MACE was significantly worse with HCR in high-risk patients. Our results are consistent with the findings of previous meta-analyses[13–15]; although Phan et al[13] found a lower rate of MI in the HCR group, it should be noted that meta-analysis only included 8 studies compared with the 14 in this meta-analysis. In the longer term (at 18 months) it has been reported that HCR was significantly favored for MACCE[21]; whereas, although MACCE was similar at 30 months, the stroke rate was significantly lower in the HCR group.[23] These findings suggest that HCR is safe and in the mid-long term may offer significant benefits compared with conventional CABG.

Ventilation time was shorter in the HCR patients. It has been reported that shorter extubation time reduces the risk of ventilator-acquired pneumonia, improves rehabilitation, and decreases ICU stays.[29] This is consistent with the trend toward a shorter ICU time that was observed in the HCR group. The shorter ventilation time may also be due to the minimally invasive nature of the LIMA to LAD surgery.[6]

4.1. Limitations

Only one of the 14 included studies in this meta-analysis was a randomized trial.[20] The remainder were nonrandomized. This introduces the possibility of selection bias. In addition, several of the funnel plots were asymmetric suggesting the added possibility of publication bias in some measurements. This meta-analysis is also constrained by the small sample size in several of the included studies with 5 studies containing <100 patients.[11–12,17–19]

The approach used to carry out the conventional CABG varied among surgeons with some using off pump,[9,11–12,17,21,23,25] some on-pump,[18,22] and others leaving it to the surgeon's preference.[10,16,19–20] It is known that in the short term (<30 days) off pump may have better clinical outcomes[30]; however, in the longer term (5 years) on-pump is significantly favored in terms of mortality.[31]

There were also differences in the timing of the PCI after the LIMA to LAD surgery among the different studies. In most cases the surgery and PCI were carried out on the same day; however, in 2 cases the PCI was carried out after 21 hours[20] or 48 hours.[19]

Finally, there were differences in the approach used to perform the LIMA to LAD surgery. This included the use of robotics[17] or endoscopic approaches[9–10,20] and the precise location of the minimally invasive incision (e.g., ministernotomy[16] vs anterior lateral small thoracotomy).[12]

5. Conclusions

In the short term, HCR is as safe as conventional CABG and may offer certain benefits such as a lower requirement for blood transfusion and shorter hospital stays. However, HCR is more expensive than conventional CABG.

Author contributions

Conceptualization: Nicola King.
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Formal analysis: Alexander Reynolds, Nicola King.
Investigation: Nicola King.
Methodology: Alexander Reynolds, Nicola King.
Project administration: Nicola King.
Software: Alexander Reynolds.
Supervision: Nicola King.
Validation: Nicola King.
Visualization: Nicola King.
Writing – original draft: Alexander Reynolds, Nicola King.
Writing – review & editing: Nicola King.

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